136. A method according to claim 55, wherein the one or more target nucleotide sequences are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, comprising probe sets specifically designed for the marker target nucleotide sequences, wherein one or both oligonucleotide probes in each particular set are blocked at their non-ligating ends, wherein oligonucleotide probe sets in the same group comprise either (a) the same 5' upstream primer-specific portion or (b) the same 3' downstream primer-specific portion, or (c) both the same 5' upstream primer-specific portion and the same 3' downstream primer-specific portion, said ligase detection reaction mixture further comprising the marker target nucleotide sequences and the probe sets including probe sets specifically designed for the marker target nucleotide sequences, said method further comprising:

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providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more oligonucleotide primer sets, wherein the oligonucleotide primer sets in each group comprise either the same 5' upstream primer or the same 3' downstream primer or both the same 5' upstream primer and the same 3' downstream primer, a group of oligonucleotide primers being useful to amplify all ligation product sequences in a given group;

quantifying the amount of extension products after said detecting; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the level of one or more target nucleotide sequences in the sample.

137. A method according to claim 10, wherein one primer comprises a detectable reporter label and the other primer comprises an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, said method further comprising:

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providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions and

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, wherein said detecting indicates the presence of extension products captured at particular sites to identify one or more target nucleotide sequences in the sample.

14 ~~38~~ 13. A method according to claim ~~37~~, wherein the one or more different target sequences are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, one primer comprising a detectable reporter label and the other primer comprising an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, and the oligonucleotide primer sets in the same group comprise either the same 5' upstream primer or the same 3' downstream primer, wherein a group of oligonucleotide primers may be used to amplify all ligation product sequences in a given group, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, including probe sets specifically designed for the marker target nucleotide sequences, wherein one or both oligonucleotide probe sets in the same group comprise either the same 5' upstream primer-specific portion or the same 3' downstream primer-specific portion;

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more oligonucleotide primer sets, wherein the oligonucleotide primer sets in the same group comprise either the same 5' upstream primer or the same 3' downstream primer and a group of oligonucleotide primers are used to amplify all ligation product sequences in a group;

blending the marker target nucleotide sequences and probe sets specifically designed for the marker target nucleotide sequences with the ligase detection reaction mixture;

quantifying the amount of extension products; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the level of one or more target nucleotide sequences in the sample.

15 ~~39~~. A method according to claim 1, wherein one or both oligonucleotide probes in each particular set comprise deoxy-uracil in place of deoxy-thymidine with the deoxy-uracil rendering the oligonucleotide probes and their ligation product sequences substantially sensitive to uracil N-glycosylase, said method further comprising:

blending the ligase detection reaction mixture, after said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles and before said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, with one or a plurality of the downstream primers complementary to the 3' downstream primer-specific portion of the ligation product sequences, and the polymerase to form an extension mixture;

subjecting the extension mixture to a hybridization treatment, wherein the downstream primer hybridizes to the 3' downstream primer-specific portion of the ligation product sequence and extends to form an extension product complementary to the ligation product sequence;

inactivating the polymerase;

blending the extension mixture, after said inactivating, with uracil N-glycosylase to form a uracil N-glycosylase digestion mixture;

subjecting the extension mixture to uracil-N-glycosylase digestion substantially to destroy oligonucleotide probes, ligation product sequences, and extension products generated from original target which use the 5' upstream primer as primers, without destroying the 3' downstream primer extension product generated from the ligation product sequences;

inactivating the uracil N-glycosylase;

blending, after said inactivating the uracil N-glycosylase, a polymerase with the uracil N-glycosylase digestion mixture to form the polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to the one or more polymerase chain reaction cycles to form an extension product in the first cycle which is

substantially the same as the ligation product sequence except comprising deoxy-thymidine in place of deoxy-uracil, and, in subsequent cycles, the 5' upstream primer hybridizes to the 5' upstream primer-specific portion of the extension product complementary to the ligation product sequence and the 3' downstream primer hybridizes to the 3' downstream portion of the extension product sequence which is substantially the same as the ligation product sequence, an extension treatment, whereby said subjecting the extension mixture to uracil N-glycosylase digestion substantially reduces the quantity of the ligation product sequences, either one or both oligonucleotide probes, and, thus, ligation independent extension products from said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles.

16 ~~60~~ 15. A method according to claim ~~59~~, wherein the ligation product sequences of oligonucleotide probes in a particular set generates a unique length product which is distinguishable from either probes or other ligation product sequences, said method further comprising:

C1 cont.

separating the extension products by size or electrophoretic mobility, wherein said detecting differentiates the extension products which differ in size.

17 ~~61~~. 16. A method according to claim ~~60~~, wherein the one or more target nucleotide sequences are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or more marker-specific oligonucleotide probe sets, each set comprising (a) a first oligonucleotide probe comprising a target-specific portion and a 5' upstream primer-specific portion and (b) a second oligonucleotide probe comprising a target-specific portion and a 3' downstream primer-specific portion, wherein one or both oligonucleotide probes in each particular set comprise deoxy-uracil in place of deoxy-thymidine, wherein the oligonucleotide probes in each particular set are suitable for ligation together when hybridized to a corresponding marker target nucleotide sequence, but, when hybridized to any other nucleotide sequence present in the sample or added marker sequences, have a mismatch which interferes with such ligation, said oligonucleotide probe sets and said marker-specific oligonucleotide sets forming a plurality of oligonucleotide

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probe groups, wherein the ligation product sequence of oligonucleotide probes in each particular set generates a unique length product, and thus may be distinguished from either probes or other ligation product sequences in the same group or other groups;

blending the marker target nucleotide sequences and the probe sets specifically designed for the marker target nucleotide sequences with the ligase detection mixture;

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more of the oligonucleotide primer sets, wherein oligonucleotide primer sets in the same group comprise either the same 5' upstream primer or the same 3' downstream primer, or both the same 5' upstream primer and the same 3' downstream primer, wherein a group of oligonucleotide primers may be used to amplify all the ligation product sequences in a given group;

separating the extension products by size or electrophoretic mobility;

quantifying the amount of extension products after said detecting; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to prove a quantitative measure of the level of one or more target nucleotide sequences in the sample.

18 82. A method according to claim 15, wherein, in each primer set, one primer comprises a detectable reporter label and the other primer comprises an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture of one or more polymerase chain reaction cycles, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the array-specific portions and

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, wherein said detecting indicates the presence of extension products.

19 ~~63~~. A method according to claim ~~62~~ 18, wherein the one or more different target nucleotide sequences are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, including probe sets specifically designed for the marker target nucleotide sequences, wherein the ligation product sequences of oligonucleotide probes in each particular set may be distinguished from either probes or other ligation product sequences in the same group or other groups;

blending the marker target nucleotide sequences and the probe sets specifically designed for the marker target nucleotide sequences with the ligase detection mixture;

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more of the oligonucleotide primer sets, wherein oligonucleotide primer sets in the same group comprise either the same 5' upstream primer or the same 3' downstream primer, wherein a group of oligonucleotide primers may be used to amplify all ligation product sequences in a given group;

quantifying the amount of extension products; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the level of one or more target nucleotide sequences in the sample.

C1 cont.

20 ~~64~~. A method according to claim 1, wherein each cycle of the ligase detection reaction is from about 30 seconds to about five minutes long.

21 ~~65~~. A method according to claim 1, wherein said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles is repeated for 2 to 50 cycles.

22 ~~66~~. A method according to claim 1, wherein total time for said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles is 1 to 250 minutes.

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23 ~~67~~. A method according to claim 1, wherein the ligase is selected from the group consisting of *Thermus aquaticus* ligase, *Thermus thermophilus* ligase, *E. coli* ligase, T4 ligase, and *Pyrococcus* ligase.

C1 Cont.

24 ~~68~~. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probes each have a hybridization temperature of 50-85°C.

25 ~~69~~. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probes are 20 to 28 nucleotides long.

26 ~~70~~. A method according to claim 1, wherein the oligonucleotide probe sets are selected from the group consisting of ribonucleotides, deoxyribonucleotides, modified ribonucleotides, modified deoxyribonucleotides, modified phosphate-sugar backbone oligonucleotides, nucleotide analogues, and mixtures thereof.

Please amend claims 1-10 as follows:

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1. (Amended) A method for identifying one or more different target nucleotide sequences comprising:

providing a sample potentially containing one or more target nucleotide sequences comprising sequence differences;

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providing one or more oligonucleotide probe sets, each set comprising (a) a first oligonucleotide probe comprising a target-specific portion and a 5' upstream primer-specific portion and (b) a second oligonucleotide probe comprising a target-specific portion and a 3' downstream primer-specific portion, wherein the first and second oligonucleotide probes in each particular set are suitable for ligation together when hybridized on a corresponding target nucleotide sequence, but have a mismatch which interferes with such ligation when first and second oligonucleotide probes are hybridized to any other nucleotide sequence present in the sample;

providing a ligase;

blending the sample, the one or more oligonucleotide probe sets, and the ligase to form a ligase detection reaction mixture;

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subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles to form a ligation product sequence comprising (a) the 5' upstream primer specific portion, (b) the target-specific portions, and (c) the 3' downstream primer-specific portion, when the respective target nucleotide sequence of the corresponding oligonucleotide probe set is present in the sample;

providing one or a plurality of oligonucleotide primer sets, each set comprising (a) an upstream primer containing the same sequence as the 5' upstream primer-specific portion of the ligation product sequence and (b) a downstream primer complementary to the 3' downstream primer-specific portion of the ligation product sequence;

providing a polymerase;

blending the ligase detection reaction mixture with the one or a plurality of oligonucleotide primer sets, and the polymerase to form a polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles to form extension products comprising the ligation product sequence and/or complements thereof; and

C2 cont.

detecting the extension products to identify one or more target nucleotide sequences in the sample.

2. (Amended) A method according to claim 1, wherein one of the oligonucleotide probes in each set comprises a restriction site, said method further comprising:

restriction digesting each extension product at the restriction site to produce extension product fragments, wherein the restriction site is positioned in each of the oligonucleotide probe sets to produce an extension product fragment with a unique length so that it can be distinguished from other nucleic acids in the polymerase chain reaction mixture after said restriction digesting; and

separating the extension product fragments by size or electrophoretic mobility, wherein said detecting differentiates the extension product fragments which differ in size.

3. (Amended) A method according to claim 1, wherein the ligation product sequence of the oligonucleotide probes in each particular set produces an extension product of unique length, said method further comprising:

separating the extension products by size or electrophoretic mobility, wherein said detecting differentiates the extension products which differ in size.

4. (Amended) A method according to claim 1, wherein the oligonucleotide probes in each set are configured so that the sequence of the ligation product sequence from each oligonucleotide probe set is unique and can be distinguished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the unique nucleotide sequences of given probe sets;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, wherein said detecting indicates the presence of extension products captured using the unique nucleotide sequence portions to identify one or more target nucleotide sequences in the sample.

C2 cont.

5. (Amended) A method according to claim 1, wherein, in each primer set, one primer comprises a detectable reporter label and the other primer comprises an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, wherein said detecting indicates the presence of extension products captured at particular sites to identify one or more target nucleotide sequences in the sample.

6. (Amended) A method according to claim 1, wherein the relative amounts of two or more differing sequences are present in a sample in unknown amounts

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with a plurality of target nucleotide sequences being quantified and a set of oligonucleotide primers being useful in amplifying all the ligation product sequences formed by the oligonucleotide probe sets in each particular probe group, the oligonucleotide probe sets forming a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, wherein oligonucleotide probe sets in the same group comprise the same 5' upstream primer-specific portion and the same 3' downstream primer-specific portion, said method further comprising:

quantifying the relative amount of the extension products, after said detecting and

comparing relative amounts of the extension products generated to provide a quantitative measure of the relative level of the two or more target nucleotide sequences in the sample.

7. (Amended) A method according to claim 6, wherein one of the oligonucleotide probes in each set comprises a restriction site, said method further comprising:

C8 cont.

restriction digesting the extension products at the restriction site to produce extension product fragments, wherein the restriction site is positioned in each of the oligonucleotide probe sets to produce an extension product fragment with a unique length so that it can be distinguished from other nucleic acids in the polymerase chain reaction mixture after said restriction digesting; and

separating the extension product fragments by size or electrophoretic mobility, wherein said detecting is carried out by size differences in the extension product fragments.

8. (Amended) A method according to claim 6, wherein oligonucleotide probe sets in the same group comprise the same 5' upstream primer-specific portion and the same 3' downstream primer-specific portion, and the ligation product sequences of oligonucleotide probes in each particular set have a unique length product so that they can be distinguished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

separating the extension products by size or electrophoretic mobility, wherein said detecting is carried out by size differences in the extension products.

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9. (Amended) A method according to claim 6, wherein the ligation product sequences of oligonucleotide probes in each particular set comprise unique sequences so that they can be distinguished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the unique nucleotide sequences of given probe sets;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner; and

detecting the presence of extension products captured at particular sites.

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10. (Amended) A method according to claim 1, wherein one or both oligonucleotide probes in each particular set comprise blocking groups at their non-ligating ends with blocking group rendering the ligation product sequence of the oligonucleotide probes in a particular set substantially resistant to exonuclease digestion, said method further comprising:

subjecting the ligase detection reaction mixture to exonuclease digestion after said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles and

inactivating the exonuclease.

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